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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/726,899	11/29/2000	Olga Bandman	PF-0187-2 DIV	3562

27904 7590 07/28/2003

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/726,899	Applicant(s) BANDMAN ET AL.
	Examiner Jessica H. Roark	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/29/2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/6/03 (Paper No. 19), is acknowledged.
Claim 14 has been cancelled previously.
Claim 1 has been amended.
Claims 1-13 *are pending.*

2. Claims 1-11 with respect to SEQ ID NOS:1, 5 and 7, and claims 12-13 in full are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 4.

Applicant's continued traversal of the restriction requirement and request for rejoinder are acknowledged.

The restriction requirement was made Final in Paper No. 6 for the reasons set forth therein.

Claims 1-11 (only with respect to SEQ ID NO:3) *are under consideration in the instant application.*

In order to facilitate the prosecution of this application, Applicant is requested to consider amending the claims to delete the non-elected embodiments from the claims.

3. This Office Action will be in response to applicant's arguments, filed 5/6/03 (Paper No. 19). The rejections of record can be found in previous Office Actions (Paper Nos. 6, 9 and 18).

It is noted that New Grounds of Rejection are set forth herein.

Claim Rejections - 35 USC § 112 first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-2 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody to the full length polypeptide of SEQ ID NO:3 or an immunogenic fragment thereof; does not reasonably provide enablement for an antibody to a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3" wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record may be found in full in Paper No. 18 and *is hereby incorporated as if set forth in full.*

Applicant's arguments, filed 5/6/03 have been fully considered but have not been found convincing essentially for the reasons of record. It is noted that the amendment filed 5/6/03 does not appear to alter the rejection of record.

Applicant argues that the specification provides sufficient guidance as to how to make a naturally-occurring amino acid sequence that is at least 90% identical to SEQ ID NO:3 because the specification teaches how to find naturally-occurring polynucleotide variants and determine if the encoded amino acid sequence is at least 90% identical. Applicant then argues that, given any polypeptide, no undue experimentation would be required to make and use and antibody that binds that particular polypeptide in view of the guidance provided in the specification as filed.

However, for the reasons of record (e.g., Paper No. 18, Section 7) the specification does not provide sufficient guidance as to how to make and use an antibody to polypeptides that are "naturally-occurring" variants of SEQ ID NO:3 comprising at least 90% identity over the full length of SEQ ID NO:3, irrespective of the recitation that the polypeptides support NADH dehydrogenase activity.

While an antibody may be made that binds essentially any protein, either the protein of interest, or a protein which shares an antibody epitope with the protein of interest, is required to make the antibody.

In the instant case, the only naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:3 disclosed in the specification is the polypeptide of SEQ ID NO:3. While as noted in Paper No. 18 hybridization and other assays might be used to isolate DNAs encoding other naturally-occurring amino acid sequences having at least 90% sequence identity to the sequence of SEQ ID NO:3, the ability to "make" these polypeptide variants by isolating the DNA encoding them and characterizing their level of percent identity to SEQ ID NO:3 requires that it be predictable that such sequences exist. Experimentation is undue when there is insufficient basis for predicting that other members of the genus recited exists.

Neither the specification nor the state of the art provides other naturally-occurring sequences meeting the criteria recited in the instant claims. Thus the instant claims are essentially a "wish to know" the identity of any polypeptide which is naturally occurring and has at least 90% amino acid sequence identity to the polypeptide of SEQ ID NO:3 so that an antibody can then be prepared to it. It has been previously decided that claims recitations so broad do not provide sufficient guidance as to how to make and use the claimed invention. See Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

It is further noted that a claim that recites an antibody to SEQ ID NO:3 is already a claim to a genus of antibodies because multiple epitopes are contained within the structure of the polypeptide of SEQ ID NO:3. The scope of the claim is extended greatly by permitting variation in the sequence of the antigen, even only 10% variation, because insufficient guidance has been provided as to the epitopes (i.e., the amino acid sequences of the protein which are actually contacted by the antibody) of SEQ ID NO:3.

Thus the Examiner maintains for the reasons of record that the specification does not appear to provide sufficient guidance such that the skilled artisan is enabled to make and use an antibody to the recited polypeptides commensurate in scope with the instant claims. Because there is reason to doubt that the scope of enablement (antibodies to the polypeptide of SEQ ID NO:3 and fragments thereof) is commensurate with the scope claimed (any antibody that binds any naturally-occurring polypeptide at least 90% identical to SEQ ID NO:3).

6. Claims 1-2 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The rejection of record may be found in full in Paper No. 18 and *is hereby incorporated as if set forth in full.*

Applicant's arguments, filed 5/6/03 have been fully considered but have not been found convincing essentially for the reasons of record. It is noted that the amendment filed 5/6/03 does not appear to alter the rejection of record.

Applicant argues that the Examiner has failed to take into account what is now claimed, and that the specification provides an adequate written description of an antibody to a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3" wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity because both a structural basis (90% identity to SEQ ID NO:3) and a correlative function has been provides for the polypeptide. Applicant concludes that since the variant polypeptides are adequately described, antibodies to these polypeptides are adequately described.

As previously noted, a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3" wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity is a recitation of a genus of polypeptides for which Applicant has disclosed a single species: the polypeptide of SEQ ID NO:3.

The claims recite that the polypeptide to which the antibody binds is "naturally-occurring" and has a testable function of "NADH dehydrogenase activity". The specification proposes that other members of the "naturally-occurring" polypeptide genus may be identified by using hybridization probes to identify DNAs or RNAs related to the nucleic acid encoding SEQ ID NO:3, expressing the polypeptide, and assaying the polypeptide for NADH dehydrogenase activity (see pages 50-52 in particular).

However, Applicant does not appear to have provided a description of which polypeptide sequences are "naturally-occurring", even among those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO:3. Neither does Applicant appear to have provided a description of how the structure of the polypeptide of SEQ ID NO:3 relates to the structure of other "naturally-occurring" polypeptides which have NADH dehydrogenase activity, even for those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO:3. Thus the Examiner maintains that neither the common attributes of the genus nor the identifying attributes of individual species other than SEQ ID NO:3 appear to have been described.

The invention now claimed is any antibody to any polypeptide that is naturally-occurring, has at least 90% identity to SEQ ID NO:3, and supports NADH dehydrogenase activity. For the reasons of record and as set forth supra Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds. Thus the Examiner maintains that Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides.

35 U.S.C. §§ 102 and 103

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Bentlage et al. (Biochimica Biophysica Acta 1995; 1234:63-73, of record).

Applicant's arguments, filed 5/6/03, have been fully considered but have not been found convincing, essentially for the reasons of record in Paper Nos. 6, 9 and 18. It is noted that the amendment to claim 1 filed 5/6/03 does not appear to alter the rejection of record.

Applicant again argues that because the claims require that the antibody "specifically bind" a particular sequence, the instant claims are not anticipated by the teachings of Bentlage et al.

It is again noted that this rejection does not necessarily rely on the fact that an antibody may "specifically bind" more than one polypeptide that shares the epitope recognized by the antibody, although as discussed more fully in Paper No. 9 such binding is indeed still specific. For the reasons of record the Examiner disagrees with Applicant's attempts to redefine the term "specifically binds", and notes that while Applicant may indeed be their own lexicographer, terms may not be defined in a manner that is repugnant to the art.

Nevertheless, arguments that attempt to limit the term "specifically binds' to binding of an antibody to ONLY that protein recited are of little relevance in the instant case because the rejection of record is based upon the evidence that Bentlage et al. teach an antibody that appears to bind a polypeptide that would inherently possess the amino acid sequence of SEQ ID NO:3 or an amino acid sequence at least 90% identical to SEQ ID NO:3.

As previously noted, Bentlage et al. teach a polyclonal antibody that binds a 15kD protein of human Complex I (see entire document, especially Section 2.4 and Figure 4a, arrowheads). Although the polypeptide of 15kD recognized by the antibodies was not shown to comprise SEQ ID NO:3; the molecular weight is consistent with that of the polypeptide of SEQ ID NO:3, and the polypeptide is part of human Complex I which is comprised of SEQ ID NO:3. Therefore, the antibodies taught by Bentlage et al. anticipate an antibody which specifically binds a polypeptide comprising the amino acid sequence of SEQ ID NO:3. *SEQ ID NO:3 would be an inherent property of the polypeptide recognized.*

Further, the polypeptide bound by the antibody of Bentlage et al. would inherently function as a NADH dehydrogenase, as evidenced by the fact that, as taught by Bentlage et al., the polypeptide is part of human Complex I and has the same size as the polypeptide of SEQ ID NO:3.

Applicant has argued in the Remarks filed 5/6/03 that because there are at least 6 different subunits of comparable amino acid sequence length or molecular mass, one cannot conclude that the polyclonal antisera of Bentlage et al. does in fact bind a polypeptide having the amino acid sequence of SEQ ID NO:3. Applicant invites the Office to show where it is taught that the 15kD Complex I subunit is the polypeptide of SEQ ID NO:3 and not one of the other Complex I subunits of similar size.

The Office is not in a position to test which polypeptides are recognized by the polyclonal antibody preparation of Bentlage et al. Applicant is again reminded that "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. In re Fitzgerald, 619 F. 2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)). (See MPEP 2112 and 2112.01).

Applicant concludes that the holo-enzyme antibody has at best a 1 in 7 chance of detecting SEQ ID NO:3, but since there is no conclusive evidence that it does so the teachings of Bentlage et al. cannot anticipate the instant claims.

The Examiner does not deny that post filing date evidence indicates that there are a total of 7 nuclear-encoded polypeptide subunits in human Complex I that have a similar size to the polypeptide of SEQ ID NO:3. However, Applicant's arguments appear to be based on the assumption that the antibodies of Bentlage et al. specifically bind only one polypeptide. The antibodies of Bentlage et al. are in the form of an antisera. There are many different individual antibodies in an antisera preparation, each specifically binding a particular polypeptide. Thus although there are multiple Complex I polypeptide subunits of approximately the same size as the polypeptide of SEQ ID NO:3 in a preparation of human tissue, nothing precludes the antisera containing antibodies to each of those polypeptides.

The fact that Bentlage et al. teach that the antisera reacted with polypeptide material of the appropriate size for the polypeptide of SEQ ID NO:3 is prima facie evidence that the antisera of Bentlage et al. includes an isolated antibody that specifically binds the polypeptide of SEQ ID NO:3. There may be other antibodies which specifically bind other polypeptide subunit of human Complex I and which contribute to the detection of polypeptides 15kD in size. There is no reason that a signal at the 15kD position of a (1-dimensional) gel does not represent binding of different antibodies to different polypeptides of 15kD. However, the presence of multiple antibody specificities in the antisera does not negate the fact that the binding of each antibody is specific, and that one or more of those antibodies in the antisera binds the polypeptide of SEQ ID NO:3.

The Examiner maintains that the reference teachings anticipate the instant claimed invention.

The rejection is maintained for the reasons of record.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al. (J. Mol. Bio. 1992;226:1051-1072, IDS #2), in view of Bentlage et al. (Biochimica Biophysica Acta 1995; 1234:63-73, of record), and in further view of Ramakrishnan et al. (US Pat No. 5,817,310, of record).

Applicant's arguments, filed 5/6/03, have been fully considered but have not been found convincing, essentially for the reasons of record in Paper Nos. 6, 9 and 18. It is noted that the amendment to claim 1 filed 5/6/03 does not appear to alter the rejection of record.

The rejection of record may be found in Paper No. 18 and is hereby incorporated by reference as if set forth in full.

Applicant argues that Walker et al. do not make up for the deficiencies discussed supra with respect to Bentlage et al. However, it is noted that Bentlage et al. is not the primary reference in the rejection of record under 35 USC 103, but rather Bentlage et al. is used to show that the ordinary artisan at the time the invention was made would have both the motivation and a reasonable expectation of success of producing the instantly claimed invention.

Applicant further notes that the B15 polypeptide taught by Walker et al. is not at least 90% identical to the polypeptide of SEQ ID NO:3, and that Walker et al. does not teach antibody epitopes of the B15 polypeptide.

The Examiner has previously acknowledged that the B15 polypeptide has 75.8% identity to the polypeptide of SEQ ID NO:3. However, the B15 polypeptide and SEQ ID NO:3 do share several stretches of amino acid identity that are 5 amino acids in length or greater. Thus the B15 polypeptide and the polypeptide of SEQ ID NO:3 do share numerous antibody epitopes. Recognition by Walker et al. of which subsequences constitute epitopes is not required since immunization with the intact polypeptide would elicit antibodies to these epitopes, and because methods of identifying those subsequences which correspond to immunogenic fragments were well known in the art at the time the invention was made.

Applicant again argues that the because the polypeptide of Walker et al. is not SEQ ID NO:3, and antibodies of the invention specifically bind SEQ ID NO:3. It is again noted that an antibody that is elicited by immunizing with one antigen nevertheless specifically binds to other polypeptides sharing the epitope bound by the antibody. In particular, as previously noted Bentlage et al. teach that antibodies produced using bovine Complex I as an immunogen react specifically with the corresponding polypeptides from human Complex I (see especially Section 2.4 and Figure 4a, arrowheads).

Applicant also argues that Bentlage et al. only teach that bovine complex I antibodies bind only some human Complex I polypeptides, not all, and that none of the subunits which might be bound by bovine complex I antibodies are identified.

The rejection of record under 35 USC 103 does not rely directly on which polypeptides of human Complex I are specifically bound by the antisera of Bentlage et al. Rather, the rejection notes that given the teaching of a bovine polypeptide subunit of complex I by Walker et al., the recognition in the art that antibodies specific for the corresponding human Complex I subunit could be produced by immunizing with bovine complex I subunits or fragment thereof, and methods of making any of a variety of types of antibodies; the ordinary artisan at the time the invention was made would have found it obvious to use the B15 polypeptide sequence or fragments thereof to produce antibodies that bound the corresponding human subunit. SEQ ID NO:3 is a corresponding human subunit in view of its 75.8% identity and numerous shared immunogenic subsequences.

As previously noted, Bentlage et al. teach antibodies and methods of producing polyclonal antibodies to polypeptide components of NADH dehydrogenase (see entire document, e.g., Abstract). Antibodies to both purified polypeptide, or to peptide fragments, are taught (e.g., see Section 2.4). Bentlage et al. teach that NADH dehydrogenase is a multi-subunit protein also known as Complex I (e.g., see Introduction on page 63). Bentlage et al. teach that antibodies against Complex I subunits are very useful for studying the molecular basis of mitochondrial encephalomyopathies (e.g., see Introduction and Discussion). Finally,

Given the teachings of Bentlage et al. that antibodies were known to be very useful for studying diseases related to defects in Complex I subunits; the ordinary artisan would have been motivated to produce antibodies to B15 and use their ability to specifically bind the corresponding human polypeptide for studies of human Complex I-associated diseases. Since methods of producing antibodies to either polypeptides or polypeptide fragments were well known in the art at the time the invention was made; the ordinary artisan would have had a reasonable expectation of success in producing such antibodies. Finally, the ordinary artisan would have been motivated to formulate the antibody in a composition comprising a pharmaceutically acceptable carrier such a PBS or water for use in any of a variety of detection assays.

Therefore, the Examiner maintains that the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection is maintained for the reasons of record.

Conclusion

11. No claim is allowed.

12. This application contains claims 1, 3, 6, 12 and13 drawn to an invention nonelected with traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

13. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
July 28, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
7/28/03
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